The National Academy of Sciences, India

MALARIA CONTROL IN THE NEXT MILLENNIUM
CHALLENGES AND OPPORTUNITIES

Presidential Address
Dr. V.P. Sharma

Sixty-Ninth Annual Session
November 11-13, 1999
Barkatullah University, Bhopal

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Malaria Control in the Next Millennium: Challenges and Opportunities

V.P. SHARMA[1]

On behalf of The National Academy of Sciences, India and on my own behalf, I extend a very warm and cordial welcome to all the distinguished participants attending the 69th Annual Session of our Academy. I wish to thank the Council and the fellowship of the National Academy of Sciences for electing me as its President, a rare distinction in my scientific career. I hope I would be able to keep up the expectations of the scientific community in furthering the objectives of the Academy. We are very grateful to Prof. M.S. Soda Vice-chancellor for inviting us to hold the Annual Session of the Academy on this beautiful campus of Barkatullah University. Our special thanks are to Prof. P.S. Bisen and all those who have worked hard to make the Annual Session a success. We are very proud of this partnership in science with Barkatullah University and hope to continue and nurture this symbiotic relationship with all the educational institutions. The Academy has a very laudable objective pf enthusing young students and scientists to enjoy the excitement of science and do good science. Our partnership with universities is to fulfil this objective. Some of you have travelled long distances and have spared your valuable time to be here, which speaks of your interest and commitment to the activities of the Academy. I hope your stay is comfortable and you would be able to enjoy the scenic beauty as well as historical landmarks, the lakes with gardens, old mosques and palaces of Bhopal.

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Introduction

In the true tradition of the National Academy of Sciences, the oldest of the science academies, with abiding concern with societal problems, the theme of my Presidential address is focussed on highlighting the challenges and opportunities that lie ahead in the control of a dreadful disease — Malaria, a major health problem.

The father of our nation, Mahatma Gandhi as early as in 1947, just when we got the independence, was concerned about the inherent problems of the society including food, water, clothing and health. He had said: " The inference we may draw is that although we may become independent in this respect, we are yet to achieve the same in our state craft as the economic plight of our teaming millions has not improved."

This is the last Annual Session of the Academy for the present millennium. The dawn of next century would raise hopes and aspirations in the people, particularly in this part of the continent. A clean, healthy, productive life for its population, rapid socio-economic development embedded in the true value systems of the country is what is called for and we all aspire for that.

Issues and Concerns

The world population has already touched 6 billion on 12th October, 1999. India will have to meet requirements of one billion people very soon. With the rapid industrialization, urbanization, better transport and communication systems, while we continuously improve our material gains, we are also heading towards some problems- the whole area of emerging and re-emerging in-

fections. Many diseases are entering the cities because of poor sanitary conditions, overcrowding, and lack of health services to cope with the expansion of towns.

Global burden of vector borne diseases such as malaria, lymphatic filariasis and dengue is given in Table 1. It is revealing that Disability Adjusted Life Years (DALY) estimated by the WHO for

Table 1. Burden of Disease (DALY) and WHO regions for 1998

WHO Region (Population)	Malaria	Filaria	Dengue
AFR (601,783)	34,506	1,691	16
AMR (802,811)			
High income (304,886)	0	0	0
Low/Middle income (497,925)	130	9	1
EMR (473,644)	1,854	126	1
EUR (870,129)			
High income (392,402)	0	0	0
Low/Middle income (477,727)	0	4	0
SEAR (1,485,056)			
India (982,223)	577	2,063	353
Others (502,833)	1,608	429	118
WPR (1,651,153)			
High income (198,497)	0	0	0
China (1,255,698)	3	232	21
Low/Middle income (196,958)	588	146	48
WHO (5,884,576)			
High income (907,828)	0	0	0
Low/Middle income (4,976,748)	39,266	4,700	558

(Source: WHO 1999, Annual Report; All figures are in 000)

1998 are confined to the low and middle income groups in all regions of the world, and there is no DALY in the high income groups (WHO, 1999). As per the Planning Commission estimates, 39% of India's population live below poverty line. Obviously in India poverty is one of the biggest driving factors in the spread of vector borne diseases. Changes in the land use pattern also create problems in the control of diseases. The publication on livable cities for the 21st century (World Bank) reports that by 2025, 88% of the world's total population growth will be located in the rapidly expanding urban areas and 90% of that growth will be absorbed by the developing world. Environmental degradation is enormous and this will have far reaching consequences on the health of urban population. Almost 70% of India's population do not have proper sanitation facilities. The untreated human waste pollutes 14 major rivers and empty 50 million cubic meters of sewage into the sea every year. The National Family Health Survey reports that 83.5% of the households in Bihar and 87.4% in Himachal Pradesh have no toilet facilities. Calcutta dumps 400 million metric tons of untreated sewage and other wastes into the Hoogly estuary and Mumbai 365 million metric tons in the Arabian Sea. In Delhi, defecation on the banks of Yamuna is estimated to be 200 million liters of raw sewage daily. Improper disposal of human excreta heavily contaminates surface and ground water. India loses one million children annually due to diarrhea and other easily preventable water borne diseases. Many communicable diseases are re-occurring due to abject poverty and unclean environment. These statistics provide a glimpse of a grim urban scenario.

The new Director General of the WHO Dr. Gro Harlem Brundtland while addressing the 51st World Health Assembly in Geneva in May, 1999 had said: "Poverty is the greatest threat to peoples' health. Ill health leads to poverty and poverty breeds ill health.

Governments must take it seriously. Childhood diseases, malnutrition, spreading infections and excess fertility, we know the results."

Scientists have been concerned with the eradication of viral, bacterial and parasitic diseases. A recent concern has been the emerging and re-emerging infections. Almost 29 of them known since 1973 are looming large on our horizon threatening the humankind. There are 20 diseases likely to re-appear. It is in this context that I would like to draw the attention of this august audience about the situation of malaria in India. In this country, we had celebrated 100 years of the discovery of malaria transmission by mosquitoes made by Sir Ronald Ross on 20, August 1897 (Chauhan and Sharma, 1998). We have come a long way since then and today the malaria control strategy is based on the highest quality of scientific research and on an interdisciplinary approach.

Malaria Situation

Malaria is a major killer disease and threatens 2400 million (about 40%) of the world's population. It is the major cause of the poverty in malaria endemic countries. World Health Organization estimates 300-500 million clinical cases and 1.5 to 2.7 million deaths annually. Malaria is still prevalent in 100 countries and *Plasmodium falciparum* that causes malignant disease is prevalent in 92 of these countries. Distribution of malaria is highly uneven. An estimated 90% cases occur in Africa south of Sahara. Outside Africa 60% cases are found in just 6 countries viz., Afghanistan, Brazil, Colombia, India, Sri Lanka and Vietnam. In 1997 annual loss due to malaria in Africa alone exceeded US $ 2 billion (WHO, 1999).

Malaria is endemic in the Asian countries. The vectors and transmission pattern differ widely among the countries and within the countries from other parts of the world e.g. Africa, south of Sahara. *Plasmodium falciparum* is increasing, and with it the problem of drug resistance. In the South East Asian region of the WHO (9 countries), malaria transmission occurs in 8 countries viz., Bangladesh, Bhutan, DPR Korea, Indonesia, India, Myanmar, Nepal and Thailand. Maldives has no indigenous transmission. India contributes 85% of malaria cases and Myanmar alone contributes 65% deaths in the SEA region. It is estimated that out of 1.4 billion population, 1.2 billion population lives in malarious areas (WHO, 1997). After the successful campaign of malaria eradication in the 1960s in the SEA region, there was widespread malaria resurgence and cases reached a peak of 7.2 million in 1976. Chloroquine resistance emerged as a major obstacle in the treatment of malaria and its control, resulting in extended morbidity and increased mortality. WHO (1997) estimates 14 million cases of drug resistant malaria in the world; the South East Asian Region contributes 6 million (30%) cases.

A study of malaria trends in India revealed that initially DDT spraying wiped out the disease; cases declined from 75 million and 0.8 million deaths to about 100,000 and no deaths by 1964. These were the days of highest achievements under the National Malaria Eradication Program (NMEP). Euphoria of success was so strong that all work on malaria was de-emphasized and resources diverted to other health programs. Research on malaria was stopped and even the one time famous Indian Journal of Malariology was terminated. Analysis of malaria situation revealed that malaria was never eradicated but had only declined to low levels to return with increased vigor (NMEP, 1986). In sixties when NMEP was heading towards malaria eradication, a major prob-

lem faced by the NMEP was DDT shortage, and for the first time resistance to DDT was reported in *Anopheles culici-facies*. Furthermore reversions from consolidation and maintenance phases coincided with the DDT shortages. In the next decade i.e. seventies these problems further multiplied and as a result malaria resurgence was widespread. For the first time in 1973 resistance to chloroquine in *Plasmodium falciparum* was detected in Assam. Deaths due to malaria re-appeared. Exophilic vector behavior became more pronounced and spraying (IRS) had poor impact on vectors. NMEP also identified hard core areas of about 51 million populations where indoor residual spraying (IRS) had failed.

In the eighties, malaria problem further aggravated and focal outbreaks were reported from a number of malaria endemic states. Deaths due to malaria were reported each year. During this period new malaria ecotypes were emerging. A glaring feature was the emergence of man made malaria. In the nineties, malaria situation in the country has deteriorated further as evidenced by the failure of insecticides in the control of transmission, and an increasing trend of mono and multi-drug resistance in *Plasmodium falciparum* (Sharma, 1996a). Malaria has returned to all those areas at one time freed from the disease (Sharma, 1998b).

In 1995 annual loss due to malaria in India was estimated between US $ 0.5 to 1.0 billion, which does not include export losses due to rejection of insecticide contaminated food (Sharma, 1996b). As we enter the next millennium malaria situation in the country has become a formidable challenge in public health. Malaria deaths became a regular feature of surveillance. Malaria epidemics started visiting the country at regular intervals. The problem of drug resistance in *Plasmodium falciparum* increased

in intensity and geographical spread. Further the emergence of *Plasmodium vivax* resistant to chloroquine was reported from a few places (Dua *et al*., 1996).

The National Anti-Malaria Program (NAMP, formerly NMEP) of the Ministry of Health, Government of India is responsible for malaria control. The incidence of malaria in India is given in Fig.1 since 1960 to the present time. In the nineties, NAMP has been reporting 2.5 to 3 million parasite positive cases and about

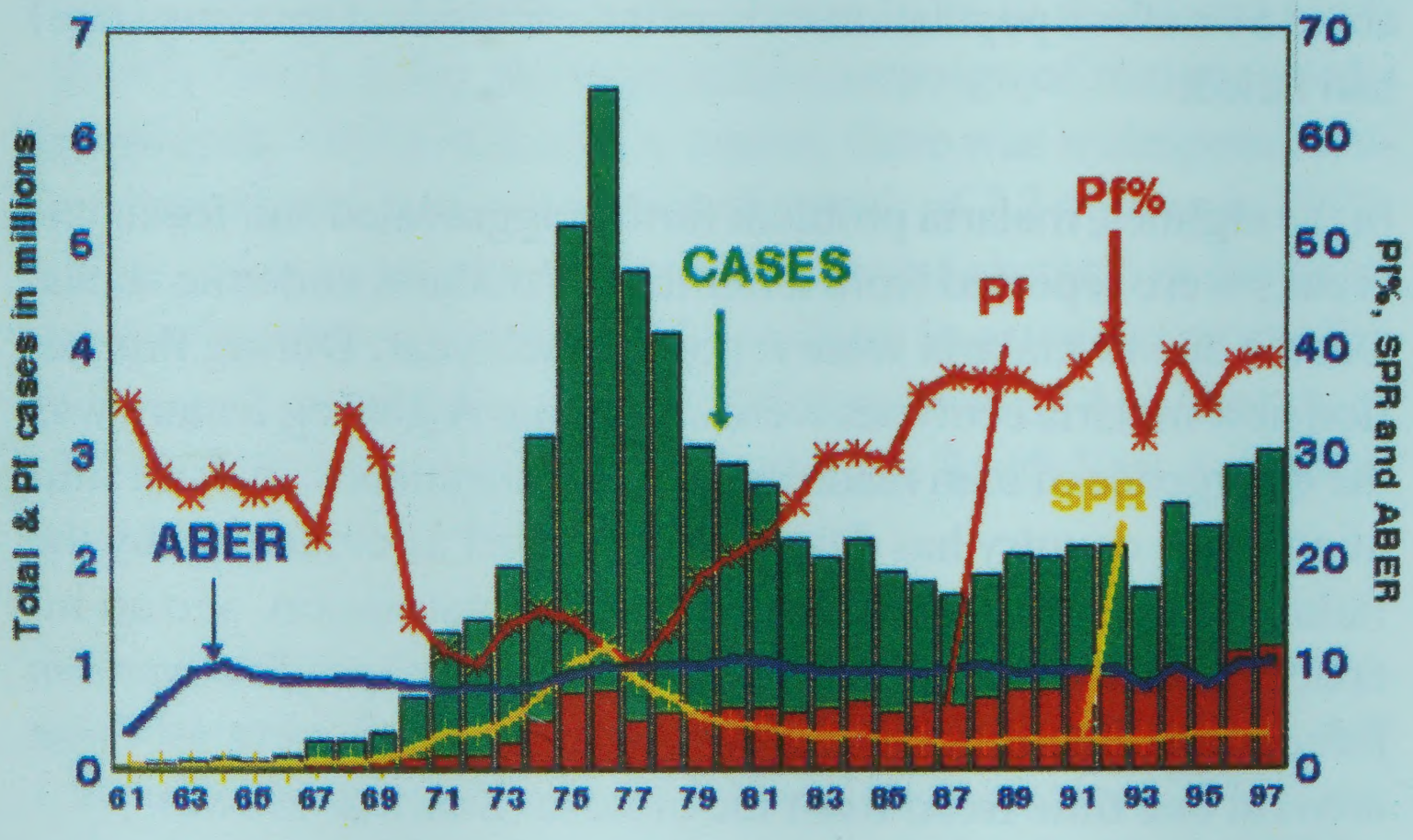

Fig.1. Epidemiological indices of malaria in India. Malaria was nearly eradicated from India by the early sixties and there were about 100,000 cases in 1965. Malaria cases multiplied and touched a figure of 6.45 million cases in 1976. Implementation of the modified plan of operation resulted in the control of malaria to about 2 million cases in the eighties, but this decline was in vivax and not in falciparum malaria. In the nineties malaria cases have again shown an increasing trend. Mortality due to malaria has increased to about 1,000 cases annually (Source: NAMP and MRC, New Delhi-110054). ABER= annual blood examination rate; SPR= slide positivity rate; Pf= *Plasmodium falciparum*.

1,000 deaths due to malaria annually (Shiv Lal *et al*., 1998). The in-depth evaluation of the National Malaria Eradication Program (now NAMP) conducted in 1985 observed that malaria incidence in the country is grossly under-reported. Incidence estimated on the basis of chloroquine consumption gave a figure of 38 million cases in 1993 (Pattanayak *et al*., 1994) and chloroquine consumption has doubled since then (Sharma, 1998a). WHO (SEARO) estimate six times more malaria cases than reported by the NAMP i.e.15 million and 19,500 deaths due to malaria in India (WHO, 1997). Unfortunately during this decade malaria situation in the country has deteriorated further as evidenced by the failure of insecticides in the control of transmission, and increasing trend of mono- and multi-drug resistance in *Plasmodium falciparum*. A recent study of the re-emergence of the diseases revealed the formation of various malaria ecotypes (Pattanayak *et al*., 1994). This was largely the result of developments under the 5-year plans creating immense opportunities for the malaria vectors to breed uninterruptedly in the man made havens. As a result, malaria at one time a rural disease has now occupied new ecotypes identified as the:

Type 1. Forest malaria: sub-type (a) malaria in the deep forests and forest fringe, vector *Anopheles dirus* — population 50 million; sub-type (b) malaria in the proximity of forest fringe and with disturbed ecology, vector *Anopheles minimus* and *Anopheles fluviatilis* — population 20 million;

Type 2 Rural malaria: sub-type (a) irrigated areas of the arid and semi-arid plains, vector *Anopheles cuicifacies* and *Anopheles fluviatilis* — population 200 million; sub-type (b) rain fed areas, vector *Anopheles culicifacies* — population 100 million;

Type 3 Urban malaria: sub-type (a) malaria in towns, vector *Anopheles stephensi* type form — population 75 million; sub-type (b) peri-urban malaria, vector *Anopheles culicifacies* and *Anopheles stephensi* type form — population 75 million;

Type 4 Industrial malaria: vector *Anopheles culicifacies* and *Anopheles stephensi* — population 10 million population;

Type 5 Border malaria: *culicifacies* — population 5 million; and

Type 6 Migration malaria: all local vectors — population 10 million.

Malaria transmission dynamics differs from one ecotype to another and therefore it is important to understand the epidemiology of malaria at the local level to institute appropriate control strategies e.g. the control of urban (Shiv Lal, 1998), forest (Kondrashin, 1992; MRC, 1991); and industrial malaria (Dua *et al*., 1997). At the international borders, malaria is already a serious problem. Porous international borders are the entry points of new strains of parasites which may be more lethal and non-responsive to the treatment. Creation of new habitats suitable for mosquito proliferation is a major emerging challenge in the new ecotypes. The next millennium has a formidable challenge in public health in the form of this disease.

Being in Bhopal let me describe briefly the malaria situation in Madhya Pradesh (M.P.). This was almost eliminated from the state. In 1961 there were only 1,180 positive and 575 *Plasmodium falciparum* cases. Malaria cases multiplied enormously in the subsequent years and in 1976 there were 8,78,693 positive and

1,55,759 *Plasmodium falciparum* cases, highest since resurgence. In the nineties malaria incidence in M.P. was 0.3 million cases (10% of the country), of which 30% constitute *Plasmodium falciparum*. In rural areas *Anopheles culicifacies* is the major malaria vector. This mosquito has acquired multiple resistant character. Elimination of this mosquito from M.P. is most difficult, as it has evolved in this region. This mosquito transmits *Plasmodium vivax, Plasmodium falciparum* and drug resistant malaria. Most efforts and finances in malaria control goes for the control of this mosquito.

An example of the impact of irrigation on malaria transmission is given in Table 2. Singh *et al.* (1997) reported that before launching of the Bargi dam over river Narmada in Madhya Pradesh, command area in Mandla were healthy but irrigation introduced malaria. Innumerable examples of irrigation schemes enhancing malaria could be cited from the country. There are many other obstacles in the successful malaria control inter alia vast inaccessible settlements; poor housing; mud plastering of sprayed walls; shortage of experienced staff etc. *Anopheles stephensi*

Table 2. Impact of Irrigation on Malaria Transmission (20 villages, Narayanganj PHC, Mandla distt.1996-97)

Indices	<14 yr.	>14 yr.	Deceased family
BSE	611	1146	45
+s	481	773	42
Pf+	437	728	42
SPR	78.7	67.4	84.21
Pf%	90.8	94.2	100.0

Ref. Neeru Singh *et al.* Current Science, 73(8):686-691, 1997.

inhabits towns and failure in its control has resulted in the rise of urban malaria. In Bhopal malaria is endemic, both *Plasmodium vivax* and *Plasmodium falciparum* are prevalent. Drug resistant strains are also encountered. Because of inadequate surveillance in the urban areas, true malaria incidence is not known. Malaria Research Centre of the ICMR has a small unit based in Jabalpur. This unit has produced good work in enhancing our understanding of malaria transmission in the forests and how it effects the tribal population. Some simple, indigenous and low cost methods of malaria control have been demonstrated in the state. I hope the state government will take advantage of these developments in malaria control.

Causative factors: I will highlight some factors responsible for deteriorating malaria situation.

Population: The population of India was 361.1 million in 1951 and life expectancy at birth was 32.1 years. The population will cross one billion on 11th May, 2000. The life expectancy has already reached 63 years. Population increase has the most profound effect on the breeding of mosquitoes that transmit various vector borne diseases. In order to sustain the population, and improve quality of life, natural resources were exploited recklessly. The environmental damage has resulted in enhanced malaria receptivity and formation of new malaria ecotypes. Population had direct impact on peri-urban settlements, expansion of towns and increase in their number. Industrialization of backward areas and wasteland in malaria endemic areas results in explosion of malaria. Industries create enormous mosquito breeding potential for *Anopheles culicifacies* and *Anopheles stephensi*. Urban expansion has contributed to the breeding of mosquitoes. Mining, railways, road construction, rural electrification, water supply in the

towns and villages, poor housing, malnutrition, migration, deforestation, cattle grazing etc. has led to the spread of malaria. Let me not misunderstood. I know how crucial it is for our country that industrialization, agriculture, and societal development proceeds at a rapid pace; but it has to be ensured that it is a holistic approach which takes care of the health problems particularly the spread of vector borne diseases.

Agriculture has changed the landscape of the hinterland. This has inadvertently brought about the introduction of many diseases e.g. malaria transmitted by *Anopheles culicifacies*. Malaria vectors that breed in agricultural fields have become resistant to insecticides e.g. *Anopheles culicifacies* breeds profusely in the irrigation system. Wherever irrigation has reached, it is often followed by a trail of malaria. Irrigation has increased from 22.6 m ha., in 1950 to >95 m ha., thus converting vast areas of the country to enhanced risk of malaria. Irrigation potential of the country is 113 m ha. therefore irrigation malaria will rise substantially unless remedial measures are in place. Punjab known for epidemic malaria, has become endemic due to irrigation. Rice fields are the main source of *Culex vishnui* mosquitoes, the vectors of Japanese Encephalitis (JE). JE epidemics have become an annual feature. Rice fields per se are not the source of malaria vectors (Sharma, 1986) but in certain areas rice agro-ecosystem provides opportunities for the malaria vectors tc breed. Urbanization and industrialization provide enormous mosquito breeding potential for *Anopheles stephensi*, the vector of malaria, *Aedes aegypti*, the vector of dengue haemorrhagic fever (DHF), *Culex quinquefasciatus*, the vector of filariasis. Thus man made ecological changes have led to the invasion of disease vectors.

Historically in India urban malaria was the problem in port cities and later invasion of *Anopheles stephensi* in towns along the riv-

ers or excessive digging of wells introduced malaria in other towns e.g. Delhi, Lucknow, Hyderabad etc. Malaria entered most of the Indian cities along with the piped water supply. Poor drainage is resulting in the uncontrolled multiplication of *Culex quinquefasciatus*, the nuisance mosquito and the vector of lymphatic filariasis. Rural water supply is leading to the invasion of *Anopheles stephensi* and *Aedes aegypti* in to villages (Gupta *et al*., 1992). In addition to malaria, dengue fever and dengue haemorrhagic fever and filariasis have become commonplace diseases and now also have been reported from rural areas. In this connection it may be noted that the possibility of the entry of yellow fever in the country has also been reported (Kalra and Sharma, 1996).

We have about 3 million new cases of malaria annually of which urban malaria cases fluctuate between 3 to 4 lakhs and accounts for 12-15% cases. Urban malaria control relies on source reduction and weekly destruction of larval breeding habitats supplemented by biological control methods, minor engineering interventions and legislative measures. Successful malaria control depends on the detection of breeding sites at weekly intervals. Due to failure in the detection and destruction of mosquito breeding, urban malaria is increasing in most of the towns of the country and now in some towns epidemic situations also prevail e.g. Navi Mumbai, Calcutta, Surat and many more. Due to population pressure, cities are expanding and new settlements in peri-urban areas have come up. An estimated 25-40% population inhabits these settlements. These peri-urban settlements often use low-lying lands, lack proper water supply and drainage. For example some estimates suggest that in Delhi 650 hutment with 15-lakh population have occupied government land illegally and these settlements lack proper civic facilities. Water is drawn with hand pump and in low-lying lands it is often contaminated leading to

epidemics of cholera and hepatitis. In this population malaria is transmitted by *Anopheles culicifacies* along with *Anopheles stephensi*. Malaria control requires indoor residual spraying (IRS) and the implementation of anti-larval methods (Kalra and Sharma, 1987).

As more people migrate to cities malaria problem is increasing and with it increases the transmission of drug resistant strains. As per the 1991 census total towns of all categories were 3,768 and malaria control is carried out in selected 133 towns with > 40,000 population. In 1991, class I and class II towns with > 50,000 population were 645. There is no information on the trend of malaria in other towns, which are not included in either urban malaria scheme (UMS) or the enhanced malaria control project (EMCP) of the NAMP. Tropical aggregation of labour is another important source of the spread of malaria e.g. in Delhi (Adak *et al*., 1994). In Panaji (Goa) malaria epidemic is the result of migrant labour imported for construction works from malaria endemic states (Kumar *et al*., 1991). Migration problem is to be seen in the background that 1/6th of the country's population migrates each year from one place to another (NMEP, 1986).

Urban and industrial malaria have become problematical because of inadequate epidemiological services; merging of NMEP units with NFCP; mosquito control is practiced rather than species sanitation; poor infrastructure and supervisory tier; inadequate finances; lack of intersectoral coordination; urban planning; urban pull leading to settlements in low lying and unhealthy areas; acute water shortage and erratic water supply; water storage in a variety of containers; poor drainage; silting of drains; floods; health impact assessment not undertaken for preventive measures; multiple authorities responsible for mosquito control; inadequate and untrained staff; legislative measures and building bye laws

either not in place or not enforced; tropical aggregation of labour; excessive drug pressure due to failure in transmission control leading to emergence of drug resistance etc. Urban vector control and reduction of mosquito nuisance can only be possible with total commitment of agencies responsible for the development and maintenance and their working together, not in isolation.

Parasite Resistance: There are four human malaria parasites. In India, *Plasmodium vivax* accounts for 60-65% cases and *Plasmodium falciparum* 30-35% cases. *Plasmodium malariae* is also encountered in some foot hill areas but its percentage is low, say about 2-3% in the area of its prevalence. *Plasmodium ovale* is not found in India but a variant of *P. vivax* is encountered in many places. The distribution of falciparum and vivax malaria is uneven. *Plasmodium vivax* is the first parasite to appear with the onset of rains and peaks in August. This is followed by *Plasmodium falciparum* peaking in September-October and its prevalence continues till the onset of winters. *Plasmodium falciparum* occurs all over the country but its prevalence is high in northeastern states, Orissa, and the forests in the plains (NMEP, 1986). Resistance in *Plasmodium falciparum* to chloroquine was first detected on the Thai Cambodia border in 1959. In subsequent years drug resistant strains moved towards north and west and entered India. For the first time in 1973 chloroquine resistance was detected in the Karbi Anglong district in Assam. Resistance problem is more pronounced in areas under the influence of efficient vectors e.g. in the northeastern states with *Anopheles dirus*, *Anopheles minimus* and *Anopheles fluviatilis*; in Orissa with *Anopheles fluviatilis* and in forests in the peninsular India in areas with high man mosquito contact. Chloroquine resistance in *Plasmodium falciparum* has been detected from all over the country and about 30% cases show some degree of resistance (Sharma, 1996a). It may be noted that only RI level of resistance is com-

mon, RII resistance is found in limited areas, and RIII resistance in some high transmission pockets. In areas showing >25% RII and RIII level of resistance in a PHC (sample size 30), the drug policy is changed to the use of sulfalene or sulfadoxine pyrimethamine combination drugs. In areas with resistance to sulfa drugs, mefloquine or quinine or arteether (E-Mal) anti-malarial drugs are used. These are life saving drugs and should be used when indicated. Resistance has already developed against mefloquine and there are reports of diminished sensitivity to quinine in *Plasmodium falciparum* in certain areas (Mishra, 1996). In recent years resistance has been reported in *Plasmodium vivax* to chloroquine from Mumbai, Mathura (UP), Chennai, and there are unconfirmed reports from other parts of the country (Dua *et al*., 1996). The status of drug resistance and its progressive spread in the country is shown in Fig. 2.

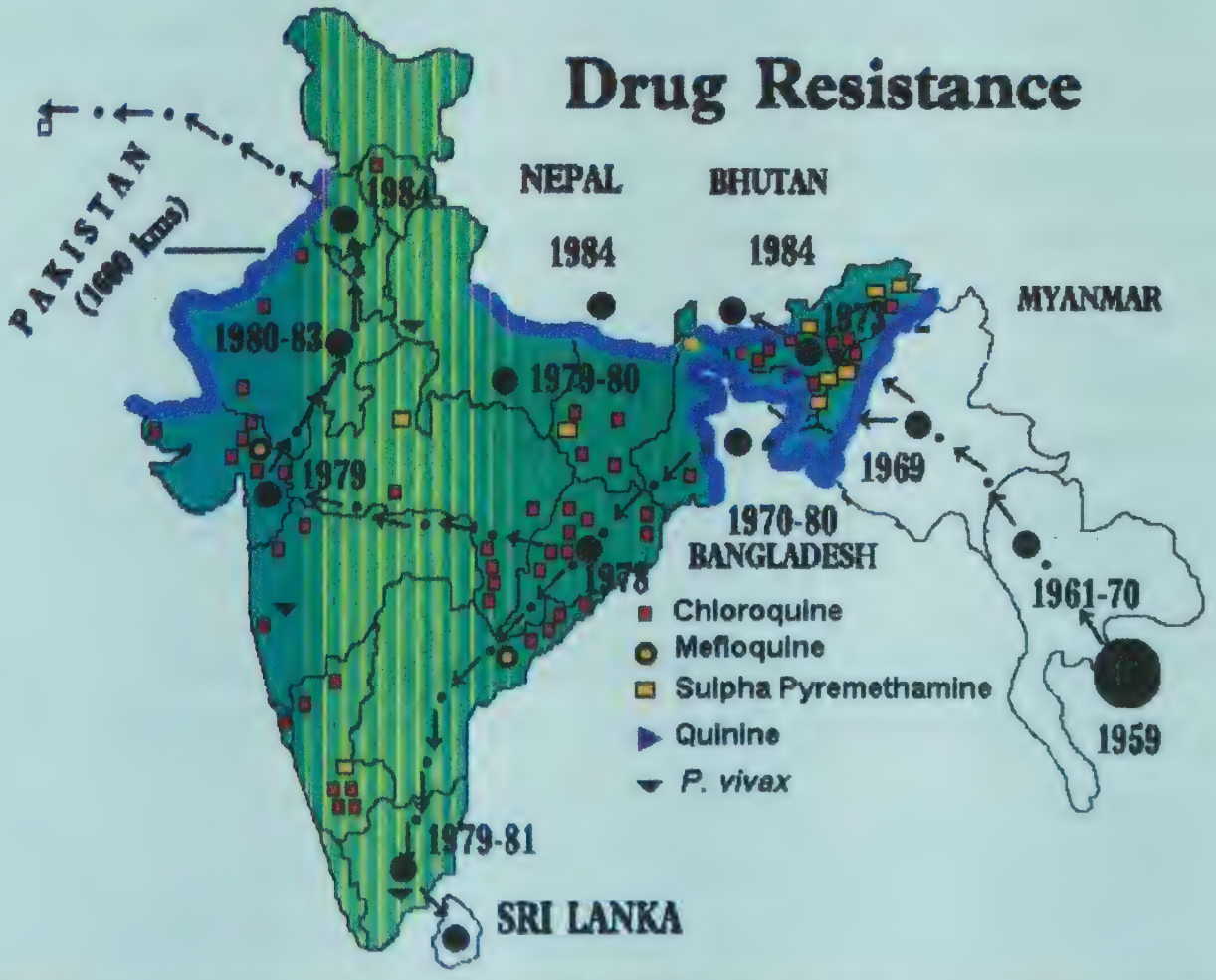

Fig.2: Status of drug resistance in the malaria parasites and its progressive spread in the country. Resistance in *Plasmodium falciparum* to chloroquine is common followed by sulfa drug resistance and the 'problem is heading towards multiple resistance. Resistance in *Plasmodium vivax* to chloroquine has also started surfacing (Source: NAMP and MRC, New Delhi-110054).

It may be noted that resistance in *Plasmodium vivax* is not monitored as is the case with *Plasmodium falciparum*. Sulfa drugs are not effective in the treatment of vivax malaria and therefore the choice of treatment would be the use of one of the life saving drugs. Large-scale use of these drugs may lead to resistance against these drugs as well. There are only limited alternative drugs in the treatment of malaria, and therefore new drugs should be introduced in the program only when it becomes absolutely essential. One implication of drug resistance is the rise in malaria related mortality by a factor of 4 to 10 or more. Furthermore the treatment of drug resistant malaria is difficult to diagnose and its treatment is 10 to 30 times more expensive. To control the spread of drug resistance, problem areas must be delimited and intensive efforts should be made to interrupt transmission. Effective insecticides should be used to control the vectors. New drugs should be introduced which are more effective. Drug policy should be revised periodically to ensure that the treatment is reliable. Private sector and NGOs must become partners in this effort to eradicate the resistant foci. The emerging challenges in parasite resistance are the increasing trend in intensity and geographical spread of resistance to anti-malarial drugs in *Plasmodium falciparum* and followed by *Plasmodium vivax*, prolonged periods of morbidity, higher mortality and high cost of treatment.

Vector Resistance: Resistance in malaria vectors to insecticides is the main obstacle in transmission control. Distribution of malaria vectors is shown in Fig.3. In India there are 58 anophelines but only 6 species are major vectors of malaria. These are the: *Anopheles culicifacies* (4 sibling species i.e. species A, B, C, and D); *Anopheles stephensi* (2 races i.e. Type form and mysorensis); *Anopheles fluviatilis* (3 sibling species i.e. species S,T and U); *Anopheles sundaicus*; *Anopheles minimus* (species A); and *Anopheles dirus* (Subbarao and Sharma, 1997). Each

sibling species differ in its biology and therefore effective vector control requires good knowledge of the biology of each sibling species, which is inadequate.

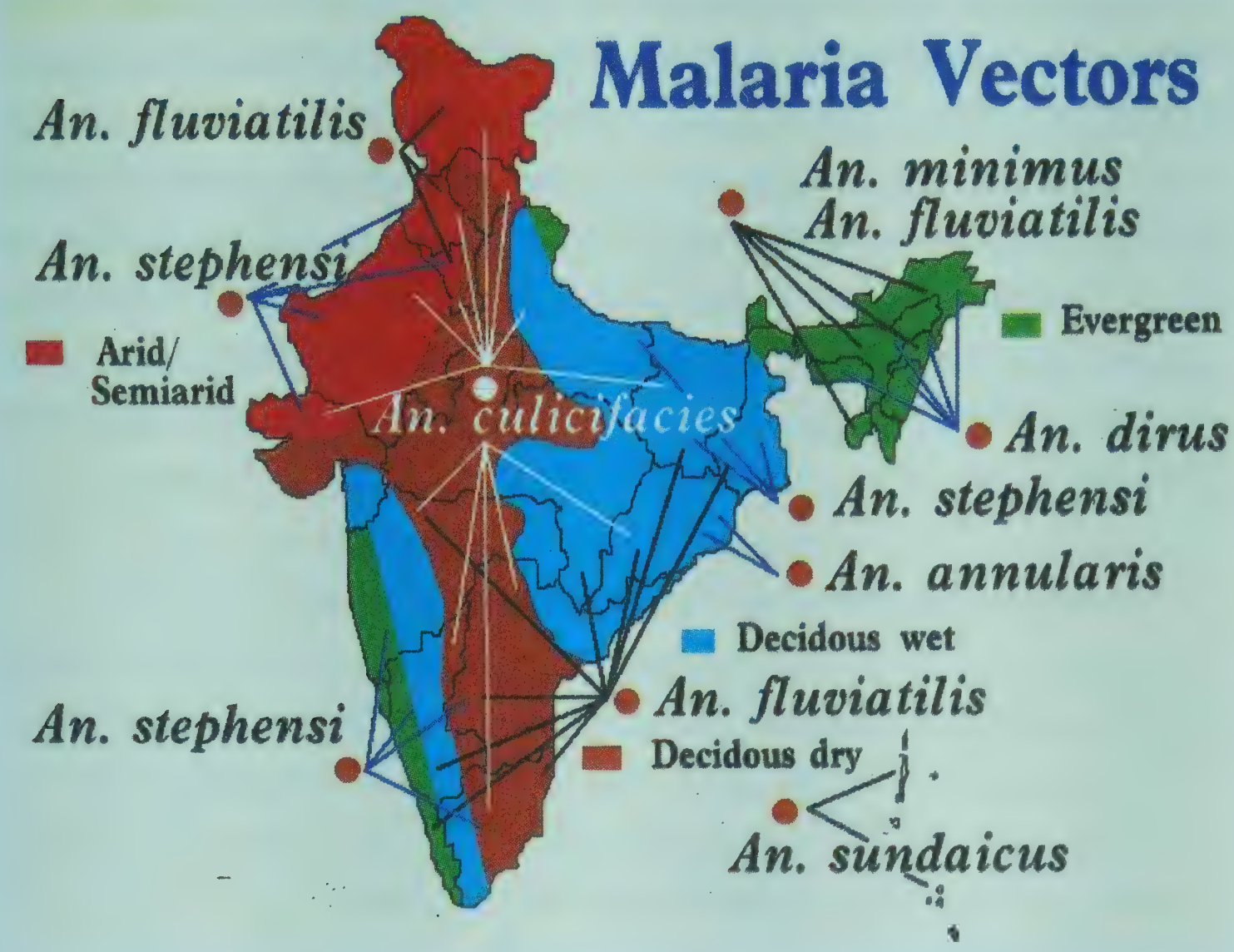

Fig. 3: Distribution of malaria vectors in India. *Anopheles culicifacies* has become triple resistant (DDT, HCH and Malathion), and this mosquito is invading new areas coming under irrigation and peri-urban settlements. *Anopheles stephensi* is entering urban and industrial settlements. These two vector account for 80% malaria transmission in the country. Other vectors limited area of influence in maintaining malaria (Source: NAMP and MRC, New Delhi-110054).

The problem of insecticide resistance is mainly confined to *Anopheles culicifacies* and *Anopheles stephensi* but in case of *Anopheles stephensi* control strategy is anti-larval, and therefore resistance is not an obstacle in its control. The vectors regulate malaria endemicity and therefore vector control is the key to successful malaria control. The main problem of malaria control

in India is the control of *Anopheles culicifacies* which has become triple resistant to insecticides (DDT, BHC, Malathion). Transmission potential of malaria vectors in India is given in Table 3. *Anopheles culicifacies* transmits 65% malaria cases and 55% are by *Plasmodium falciparum*. This mosquito transmits almost all rural malaria in peninsular India. Insecticide resistance and exophilic vector behaviour are the main obstacles in its control. The indoor residual spraying (IRS) of DDT is almost useless in achieving transmission control, BHC has been banned, Malathion has poor acceptability due to pungent odour. The trend is to spray synthetic pyrethroids (SP) i.e. cyfluthrin, deltamethrin, lambda-cyhalothrin etc. The cost of SP insecticides is 4-5 times more

Table 3. Role of vectors in malaria transmission in India

Malaria vectors	Potential to transmit malaria	Species-wise Contribution (%)	
		Malaria +s	Pf +s
Major malaria vectors of India			
An. culicifacies	+	65	55
An. stephensi	++	12	05
Major malaria vectors of regional importance in India			
An. fluviatilis	++	15	30
An. minimus	+++	5	5
An. dirus	+++	3	5
Major malaria vector of the coastal areas			
An. sundaicus	++	0.039	0.001

Source: Sharma, V.P. Current Science, 75(11):1127-1140, 1998b.

Note: Broad categorization. + low; ++ medium; +++ high., percentage calculated on the basis of 1996 malaria incidence in the country.

than DDT and therefore due to financial constraints spraying is limited to high transmission areas. An. stephensi is the vector of urban malaria. Vector control requires weekly searches of mosquito breeding habitats which is very difficult operationally. As a result *Anopheles stephensi* is maintaining high malaria transmission. *Anopheles minimus*, *Anopheles dirus* and *Anopheles fluviatilis* maintain stable malaria in the northeastern states. The vector populations are largely exophlilic. Most areas are disturbed and therefore field operations are poor and lack adequate supervision. *Anopheles fluviatilis* populations in the plains are found along the streams and maintain malaria transmission. The vector is susceptible but exophilic behaviour and operational problems result in control failures. *Anopheles sundaicus* is restricted to Andaman and Nicobar group of islands and spraying has been ineffective due to weak field operations and its exophilic behaviour. Interruption of malaria transmission was based on IRS and therefore all emphasis was given to the study of adult biology. As a result, our knowledge of larval biology remained poor. To control resistant vectors, replacement insecticides should be pressed in to service. However safer and sustainable options should be preferred e.g. bioenvironmental methods, insecticide treated mosquito nets etc. Insecticide policy should be reviewed periodically and insecticides should be selectively applied. Research should be directed to develop mitigating measures to tackle the problem of resistance. NAMP also lacks infrastructure for larval control in the rural areas. This should be established to implement bioenvironmental methods in the control of rural malaria. Challenges that lie ahead are the tackling of insecticide resistance, control of refractory malaria, prevention of the invasion of *Anopheles stephensi* and *Anopheles culicifacies* to new areas, and understanding vector biology at the local level in relation to malaria transmission and its control.

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Operational Constraints: Malaria control in the vast endemic areas requires advance planning, timely supplies, and availability of health workers during transmission. Unfortunately with the eradication of malaria expertise in malaria control (epidemiologist and vector control specialist) has been lost, and this is most pronounced in the states. Multiple agencies are involved in the procurement and supply of insecticides and drugs. Field operations of malaria control are interfered by cultural habits. In many areas it is common practice to mud plaster the walls frequently, and this practice makes the spraying ineffective. It may be noted that 7.8% population of India is tribal. This population contributes 40% total malaria cases, 60% *Plasmodium falciparum* malaria cases and >50% deaths due to malaria. Poverty, illiteracy, vocational needs of outdoor work during night, cultural habits, and human settlements etc. are conducive to high malaria receptivity and make this population highly vulnerable to malaria. Outreach of health services is poor in this segment of society. Malaria control in this population has always been most difficult and unattainable. Population settled in these areas do not want their houses to be sprayed and as a result house coverage is dismally low say about 20% or so. Malaria surveillance in general is poor as there area about 40-50% vacancies in the multi-purpose workers category. During peak transmission season the backlog of slides is generally 4-6 weeks or more.

There are serious financial constraints in the control of malaria. Government of India is spending 35% health budget in the control of malaria alone. State governments except the northeastern states have to provide 50% matching grant. Any enhanced budget for malaria control may lead to compromise on other health activities, which may not be desirable. In the last 5 years 40-50% of the targeted population received spray and this situation has not improved. In certain areas spray coverage is negligible due to

social unrest, and these areas happen to be predominantly *Plasmodium falciparum* and reports of epidemics are frequent. In 1999-2000, targeted population for spraying is 161 million; the central government is providing DDT to cover 40 million population and another 5 to 10 million population with malathion and synthetic pyrethroids.

Challenges and Opportunities: Many problems can be solved by advance planning based on stratification and mapping. Malaria control priorities should be fixed and resources diverted accordingly. Tackling societal problems will require high quality information, education and communication. Research has already demonstrated that insecticides are not the only tool for malaria control. Malaria control should use all methods wherever applicable and involve the communities, prevent the invasion of vectors and improve health delivery.

In the eighties it became clear that insecticides would not be the answer to the complex problem of malaria control. There were many reasons for that, such as insecticide resistance, exophilic vector behaviour, spraying was unsustainable and operationally difficult, spraying was harmful to human health and was polluting the environment. In many states, there were outbreaks of malaria even though these areas were under the indoor residual spraying (NMEP, 1986). Urban malaria was not responding to the methodology used under the UMS. There were epidemic situations in the country. Malaria research was accorded on high priority. The Indian Council of Medical Research has opened a permanent institute for research on malaria in 1977, i.e. Malaria Research Centre (MRC). The mandate of MRC was to provide answers to the complex problem of malaria control through research. This was a unique opportunity for focused research on malaria. New products were developed and field tested for their suitability in

malaria control. Basic, applied and field research in malaria was intensified. One outcome of this thrust was the development of bioenvironmental malaria control and related technologies. During the same period malaria control was undergoing policy changes nationally and internationally which culminated into the launching of Roll Back Malaria initiative in June 1998 by the WHO.

Research and Development: Research at MRC in collaboration with the international and national institutes of excellence have provided new tools and hope of sustainable malaria control in the country. Many technologies have been introduced in malaria control and some are in the advance stages of inclusion in the programme (NAMP). These are:

In the area of basic research: - the discovery of sibling species complex and its application in the selective vector control; - mode of inheritance of insecticide resistance; - vector incrimination using ELISA and IRMA; - computer based mosquito identification; - discovery of new molecules with anti-malaria and mosquito repellent action; - micro-dot ELISA for mosquito blood meal identification; - 3-day test for monitoring chloroquine resistance in *Plasmodium falciparum*; - Insecticide treated mosquito nets/curtains; - biolarvicides such as the *Bacillus thuringiensis* H-14, *Bacillus sphaericus* to control mosquito breeding; - large scale production of larvivorous fishes; - expanded polystyrene beads; - eucalyptus and poplar plantations to eliminate marshy areas; and - neem based mosquito repellents. - In the area of early case detection and prompt treatment:

- non-microscopic tests have become available viz., ParaSight F, and Immunochromatographic (ICT) tests; - new drugs and drug combinations have been tested and now used in the treatment of

malaria e.g. sulfa drugs have been introduced in chloroquine resistant areas; - research on Chinese herbal drug Artemisia annua has resulted in the development of arteether (E-Mal) for the treatment of serious, complicated and drug resistant malaria. This drug is now marketed; - Another anti-relapse drug CDRI 80/53 has been registered and its marketing will start soon; - new drugs are being synthesized and a few more are undergoing clinical trials; - residue analysis of insecticides has resulted in greater emphasis on alternative options in malaria control.

In the area of epidemiology: - many advances have led to our improved understanding of malaria transmission particularly in areas refractory to malaria control. - relapsing pattern of *Plasmodium vivax* has revealed strain variations in response to incubation period and primaquine; - malaria ecotypes have been identified and studies on malaria transmission dynamics are being undertaken; - remote sensing and geographical information system is being applied in the malariogenic stratification and mapping of malaria; - Techniques for the rapid assessment of malaria situation; and - cost effective malaria control strategies.

Malaria control is changing from total dependence on insecticides to integrated control with the selective application of insecticides. Intersectoral coordination and community participation are being emphasized. Legislative measures and building bye-laws are being instituted to make the communities accountable to keep their houses and surroundings free from mosquito breeding. Bioenvironmental malaria control has emerged as a major breakthrough in malaria control. Health impact assessment to prevent mosquito production is being introduced to reduce receptivity and vulnerability to malaria.

There are many challenges in research and development that should

be addressed e.g. vector biology in relation to the use of mosquito nets; vector ecology particularly of the immature stages, malaria transmission dynamics in various ecotypes; genetically modified mosquitoes refractory to transmission; mapping of malaria and factors that promote transmission to guide the interventions; safe and sustainable vector control methods, monitoring of drug resistance which should include *Plasmodium vivax*; trials with new drugs and drug combinations; low cost diagnostics; parasite biology; evolution of parasite resistance; haemoglobinopathies and malaria; pathology of malaria; clinical research; malaria vaccine and cost benefit related economic research etc.

Bioenvironmental Malaria Control: ***a success story:*** A unique, holistic and sustainable bioenvironmental approach to control malaria and other vector borne diseases emerged on the national scene as a result of concerted research. The main emphasis were on the control of mosquito breeding and prevention of mosquito bites rather than spraying of insecticides, and surveillance directed to eliminate parasite reservoir from the community. Salient features of this strategy are: (i) vector control by environmental management (environmental modification, environmental manipulation, and habitat management); biological control (fishes like guppy and Gambusia, biolarvicides); legislative measures including building bye-laws; use of personal protection methods (repellents, mosquito nets, mosquito proofing of houses, protective clothing etc.); and health impact assessment to ensure preventive vector control etc.; (ii) parasite control by early case detection through improved surveillance; prompt radical treatment; improved care of serious and complicated malaria cases; and (iii) malaria control is supported by eliciting community participation, intersectoral coordination; and information, education and communication. The strategy also involves intro-

duction of income generating and environment improvement schemes. It may be noted that insecticides are held in reserve for any emergency.

The strategy was first launched in 1984 in Nadiad Taluka, Kheda district, Gujarat. The implementation of bioenvironmental methods in the first year itself produced spectacular success in malaria control in 7 villages. Malaria cases were reduced by 94% and again by 90% in the second year. Experimental areas were gradually expanded to cover the entire Nadiad Taluka with 100 villages and 100,000 population (Sharma and Sharma, 1989; Sharma *et al*., 1991). In subsequent years more areas were brought under the new strategy. Wherever bioenvironmental interventions were applied, malaria cases showed a sharp decline. An international group of experts evaluated the project and made highly complimentary observations. The group reported that indigenous malaria transmission had ceased and malaria was controlled at much less cost and on long term basis as compared to the IRS (MRC, 1985). The strategy also produced many collateral benefits and had very high social acceptability (Gupta *et al*., 1989; Sharma 1998b). The strategy was expanded to demonstrate malaria control in areas representing various epidemiological paradigms. Implementation of bioenvironmental methods resulted in the successful malaria control in a variety of situations e.g. industrial malaria control in Bharat Heavy Electricals Ltd (BHEL), Hardwar and Indian Drugs and Pharmaceuticals Limited (IDPL), Rishikesh; coastal malaria in Car Nicobar; urban malaria in Chennai and Panjim city; rural malaria in Haldwani in the green revolution area and forest malaria in Mandla (M.P.) and near Rourkela (Orissa) Singh *et al*., 1989; Dua *et al*., 1997. The advantages of bioenvironmental methods over the chemical control are given in Table 4. The strategy of bioenvironmental malaria control was superior, cost effective and sustainable (Sharma *et al*., 1991, Sharma,

Table 4. Bioenvironmental vs. chemical malaria control strategy

Concern	Bioenvironmental control	Chemical control
1. Impact	+	–
a) Malaria	Long term	Seasonal
b) Vectors	Long term	Seasonal (R)
c) Parasite (R)	-	+
d) Human Health	+	–
e) Environment	+	–
2. Sustainability	+	–
a) Cost	Low to high	High
b) Returns	+	diminishing
c) Skills	Local	training
d) Technology	Local and universal	Sophisticated and time limited
3. Gains	+	?
a) Other Diseases	+	–
b) Development	Linked	Isolation
c) Indian ethos	+	–
d) Community	+ Response	? Response

Source: Sharma, V.P. Current Science, 75(8):756-757; 1998c.
+ = Positive; - = Negative; R = Resistance; ? = Doubtful

1991; Sharma and Sharma, 1986). Based on the field experience from various parts of the country it was concluded that the first line of attack on malaria should be the application of bioenvironmental methods, and this should also include other vector borne diseases. Chemical control methods should be used highly selective and under emergency situations.

To demonstrate the scope of this strategy in the control of endemic malaria through the primary health care system, malaria control was launched in Kamasamudram PHC in Kolar district. MRC provided technical support and work was carried out by the

state health department. Prior to the interventions, malaria cases were increasing and particularly *Plasmodium falciparum*. After the introduction of fishes malaria cases declined and reached low levels whereas malaria was increasing in the control areas sprayed with DDT. This was a clear demonstration of the useful role of fishes in malaria control as shown in Fig. 4. Based on the experience gained in Kamasamundram PHC, fieldwork was extended to demonstrate malaria control in Hassan district. In this district malaria was the main public health problem and insecticides had no place because of intensive silk culture, which is an important cottage industry. Introduction of Bioenvironmental interventions in Banavara PHC (population 56750, villages 108) eliminated vector populations and malaria cases nose-dived to very low lev-

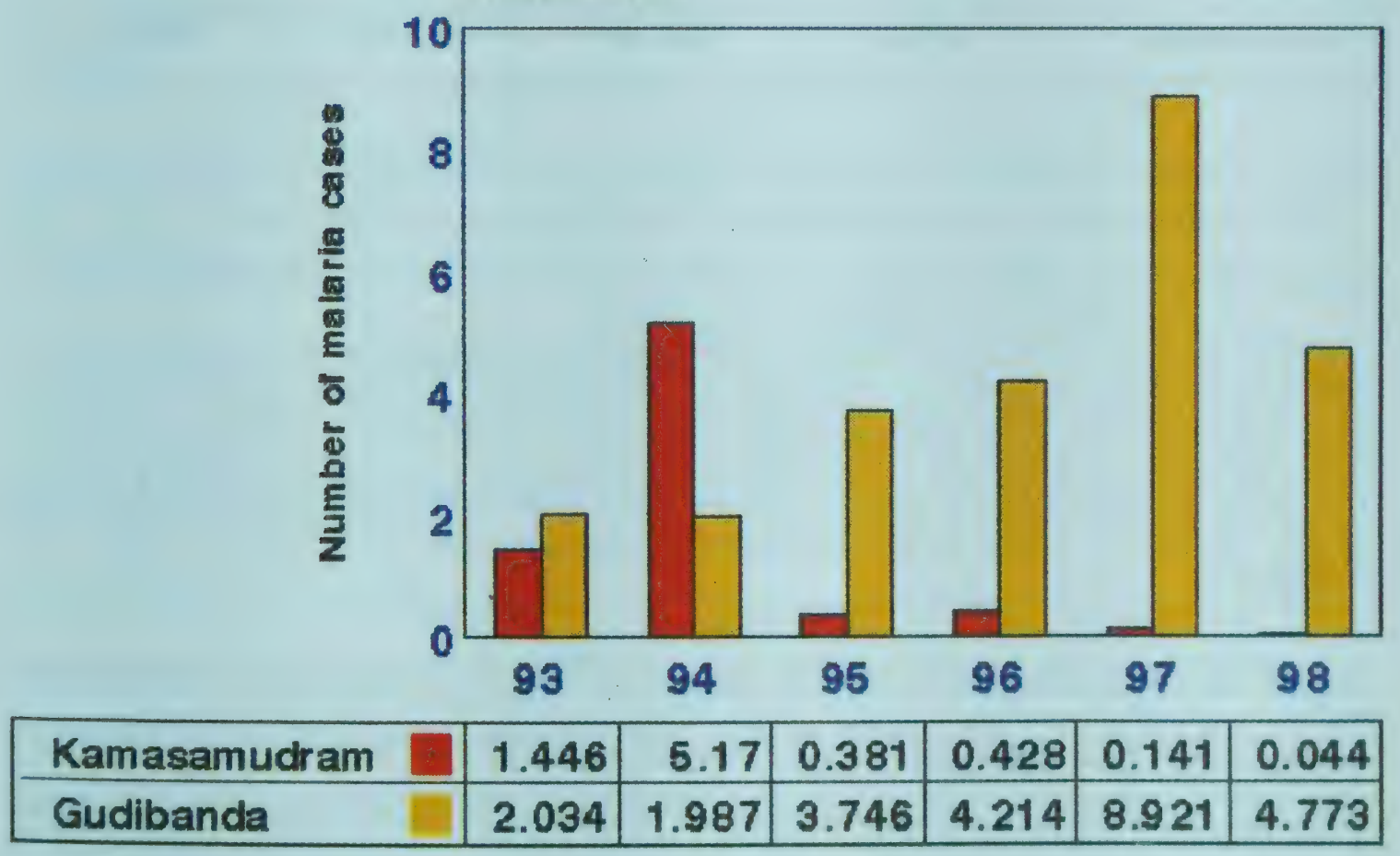
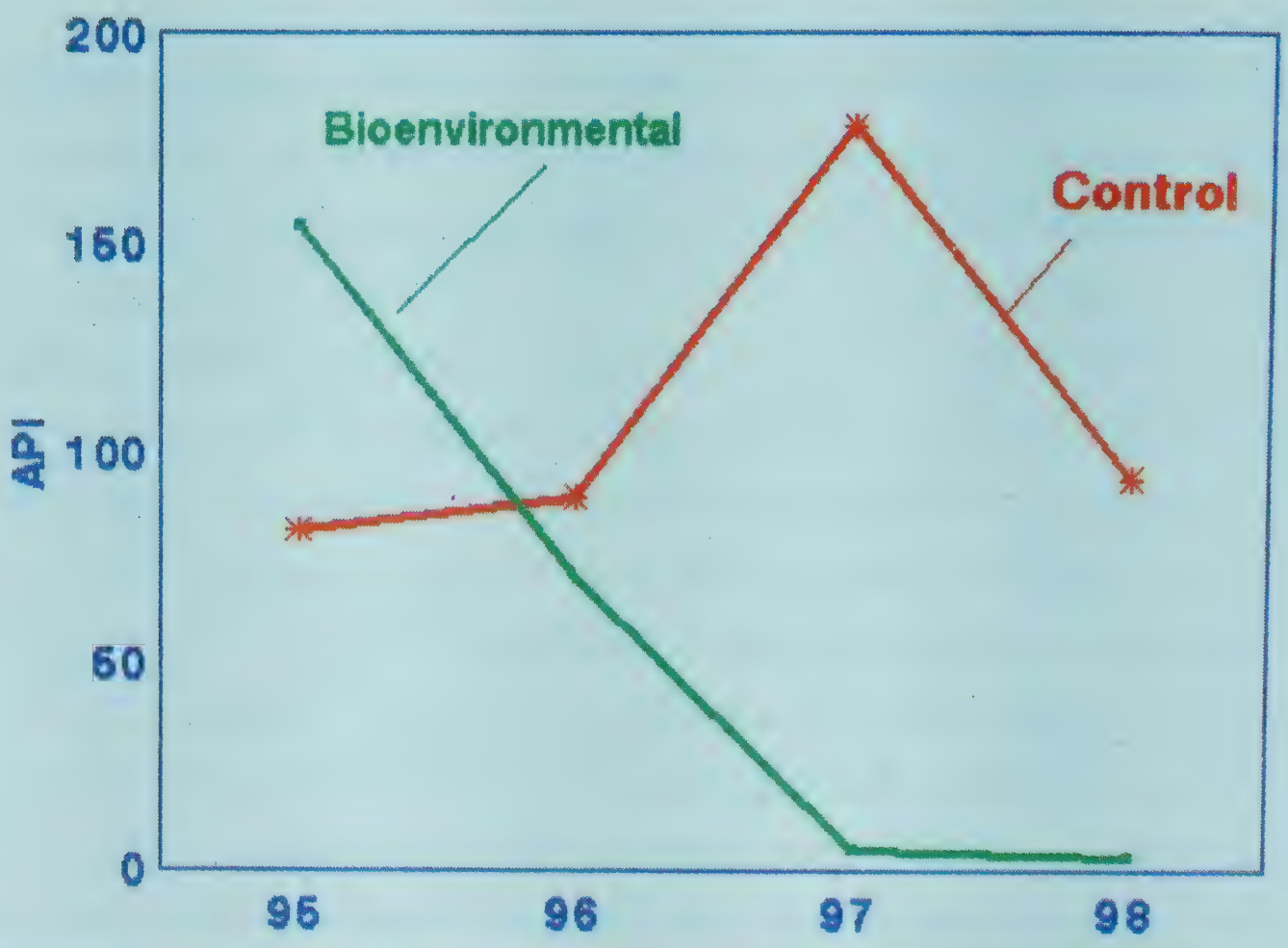


Fig. 4. Impact of bioenvironmental interventions on malaria incidence in Kamasamudram PHC and in Gudibandra PHC held as control. Malaria cases disappeared in the Kamasamudram PHC but in the control there was increase in malaria incidence (Source: S.K. Ghosh and co-workers, MRC Field Station, Bangalore).



Banavara	154.6	70	5	3.1
Gudibanda	81.3	89.3	177.9	93.8

Fig. 5: Impact of bioenvironmental strategy on malaria incidence in Banavara PHC, Hassan district, Karnataka. Malaria API fell from 154.6 in 1995 to 3.8 in 1998. In control PHC. There was increase in API. (Source: S.K. Ghosh and co-workers, MRC Field Station, Bangalore).

els as shown in Fig. 5. Bioenvironmental methods are now being applied in the control of endemic malaria in Maharashtra, Gujarat and in many urban areas like Ahmedabad, Bangalore and Chennai.

Results of field research in malaria control highlighted that in launching bioenvironmental malaria control initiative at the district level, health departments should: (i) set up intersectoral committees at the district level and ensure coordination of malaria control activities; (ii) ensure health impact assessment and provision of appropriate interventions and maintenance; (iii) institute legislative measures and building bye-laws; (iv) support community participation; and (v) prepare annual action plan

for the district and update it periodically. As stated before I wish to highlight that our first attack on malaria should be by the bioenvironmental methods followed by the integration of other methods. Insecticides would have a place but their application should be selective and when found necessary. While dealing with malaria we must realize that a massive program such as malaria control can not succeed without the active support of the people. Wherever communities will support the programme, success is bound to follow on a sustainable basis (MRC, 1986, 1993; Sharma, 1998b).

Roll Back Malaria

Dr. Gro H. Brundtland, Director General, World Health Organization launched the Roll Back Malaria (RBM) initiative in all malaria endemic countries of the world (WHO, 1999). RBM is a global initiative of the World Health Organization against malaria. RBM envisages support by the highest executive in the country and at all other levels of governance. RBM relies on the past experience and available technologies. In brief RBM envisages malaria control through the health sector development and aims at sustainable malaria control through the existing and emerging technologies. RBM is a social movement supported by many partners, targeted to reduce poverty and promote development. Many partners come together and take decisions by consensus keeping in mind the country priorities. The action plans are clear, evidence based, prioritized and adapted to local realities. RBM utilizes the existing infrastructure and available resources of malaria control to implement the six strategies i.e., (i) enhanced diagnosis and treatment of malaria e.g. new diagnostic test, universal access to treatment, combination drugs; (ii) disease transmission control (cost effective integration of vector control tools, e.g. insecticide treated nets, selective vector control, bio-envi-

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ronmental methods); (iii) enhanced surveillance (rapid response, policy making border malaria, and monitoring progress); (iv) health sector development (e.g. de-centralization, health equity, package delivering care, changing role from implementers of malaria control to leadership, regulations and coordination); (v) community mobilization (empowerment of communities, evidence based planning and ownership) and (vi) advocacy (forum for advocacy, strategic investments e.g. mapping, new drugs and vaccines, regional support networks e.g. drug policy, rapid response, etc., health impact assessment, research on reform in health system. Initially 2-year period (2000-2001) would be spent on piloting RBM at the district level followed by the extension of RBM to endemic districts.

To conclude

While working on bioenvironmental control of malaria, and trying to evolve an inter-disciplinary holistic approach I was reminded of the words of wisdom from Sir C.V. Raman, the Nobel Laureate who had said: " History of science has shown that real fundamental progress is always due to those who had ignored the boundaries of science and who had treated science as a whole." Malaria control strategy also calls for dissolving of the barriers and boundaries amongst various disciplines, and a holistic approach towards the control measures is the solution.

As we step into the new millennium malaria control has become a formidable challenge. Malaria control is a very complex undertaking, and in this connection I quote L.W. Hacket (1937) "Everything about malaria is so molded by local conditions that it becomes a thousand epidemiological puzzles. Like chess, it is played with a few pieces but is capable of an infinite variety of situations."

I do not wish to give an impression that malaria situation in the country is intractable. Based on many years of my research on malaria and that of my colleagues in MRC, I have enormous hopes and the future can be really bright for the control of this dreadful disease. Let me share with you that drugs are not the answer to malaria control. Malaria vaccines are unlikely to be soon available for mass immunization in the near future. Emergence of resistance in the malarial parasites to the drugs has complicated the treatment and reduction in morbidity and mortality due to malaria. The rational and sustainable approach to malaria control is the application of bioenvironmental methods integrated with other methods of vector and parasite control. This strategy should remain our sheet anchor to control malaria and other vector control diseases. In this connection I wish to iterate that RBM offers a unique opportunity of bringing together partners that wish to fight malaria at the global, national, regional and local level. Cost effective malaria control tools have been developed and can be applied effectively by developing local knowledge, more technologies will become available through research, resources can be mobilized, and manpower can be trained. With wholehearted political commitment and social will, sustainable malaria control is not a dream but an attainable goal. I conclude with the words of Sir Ronald Ross, one of the greatest scientist in tropical medicine- the man who demonstrated the mosquito transmission of malaria "Our duty at present is to better our present foothold; to investigate; to comprehend the forces of nature; to set our state rationally in order; to stamp down disease in body, mind and government; to lighten the monstrous misery of our fellows, not by wordy dogmas, but by calm science. The sufferings of the world are due to this, that we despise those plain earthly teachers- reason, work and discipline." Ronald Ross. Before I conclude, let me give my very best wishes to dear students and young scien-

tists, in particular. You will have to shoulder the responsibility of ushering in an era of a healthy, productive and happy human life; free of diseases, poverty and maladies. Let us try and offer remedies through a scientific approach and dedicated efforts for research and its application for the welfare of the society.

Thank you,

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